DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Cincinnati District

Food & Drug Administration
1141 Central Parkway
Cincinnati, OH 45202-1097

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

May 1, 1998

WARNING LETTER
CIN-WL-98-266

Richard B. Budde, M. D., President
Ohio Medical Instrument Co., Inc.
4900 Charlemar Drive
Cincinnati, Ohio 45227

Dear Dr. Budde:

During an inspection of your firm located at the above address by the Food and Drug Administration (FDA) our Investigators determined that your firm manufactures sterile Biopsy Kits, MRI Skull Mount Kits, and Skull Mount Kits; skull pins (sterile and non sterile); and skull clamps. These products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act). The Inspection which was conducted on March 16/April 8, 1998 revealed that your devices are adulterated within the meaning of Section 501(h) of the Act in that, the methods used in, or the facilities or controls used for manufacturing, packaging, storage, or installation are not in conformance with the Quality System Regulation (QSR) for Medical Devices specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

Failure to ensure that devices meet finished device specifications before distribution.

The following lots of devices were distributed prior to the validation of the Ethylene Oxide (ETO) sterilization process for the devices: Biopsy Kits, lot #38119395 and Skull Mount Kits, lot # 38007295 and lot # 38019395. These lots of kits were originally a part of a four and one half hours ETO validation sterilization cycle run which failed sterility testing; the lots of kits were then subjected to an additional six and one half hours ETO cycle which failed sterility testing. The lots of kits were then broken down, repackaged, and sterilized using an eight hours ETO sterilization cycle. None of these ETO sterilization cycles were validated and no product functionality or residual ETO testing was performed on the kits prior to their release for distribution.

Lot 0197 which consisted of MRI Skull Kits and Skull Mount Kits were sterilized after the validation study was completed. The lot of kits was subjected to a 10 hours ETO sterilization cycle instead of the 8 hrs.-8½ hrs. cycle that was used during validation of the ETO sterilization process. No product functionality or residual testing was performed prior to release of the kits.

Failure to adequately validate quality assurance and manufacturing operations.

The ethylene oxide sterilization process for Biopsy Kits, Skull Mount Kits, and MRI Skull Mount Kits was not adequately validated.

The validation protocol for the ETO sterilization of the Biopsy Kits, Skull Mount Kits and MRI Skull Mount Kits was not followed during the validation study. The hand drills in the kits were identified in the Validation Protocol as the most difficult to sterilize (master product) and were specified to be inoculated product for the microbiological challenge to the ETO sterilization process during the validation study. After sterility failures of the inoculated drills in the first half cycle runs of 4 hrs. and 6 hrs., inoculated drills were no longer included as a part of the validation study which included the remaining full and half cycle runs, Nos. 2, 3, & 4. Instead the syringes in the kits were identified as the master product.

No bioburden determination or USP sterility testing using specified components of the kits was performed as stated in the Sterilization Validation Protocol. No product functionality testing was performed on devices after sterilization.

Validation of the resterilization process which was performed to evaluate the feasibly of resterilization of the kits in the event of a sterility failure was not adequately completed. The syringe barrel, plunger tip and needle hubs in the Biopsy Kits were not within specifications for ethylene oxide residual when the kits were subjected to two full ETO sterilization cycles. No further studies were done to correct the problem. No product functionality testing was performed after sterilization and no post-sterilization package integrity testing on packages containing actual product was performed.

After the original validation study was completed, a sterilization validation study was conducted to adopt new type hand drills used in the kits into the validated sterilization cycle for the kits. This study did not include a determination of whether the new hand drills present a greater challenge to the sterilization process than the master product (syringes) in the previously validated sterilization process for the kits for which equivalence was being demonstrated.

The validation study to adopt the new hand drills into the sterilization cycle for the kits included only one half cycle containing the minimal load capacity ([redacted] Biopsy Kits) for the sterilization process. A sterilization cycle using the maximum (densest) load capacity ([redacted] kits) was not included in the study.

The ability of packaging for the kits to withstand expected conditions of processing, sterilization, handling, storage and distribution was not adequately validated.

The package integrity testing performed on the kits after sterilization during the validation study were performed on empty packages. No tests were performed on packages containing product.

Lot 0296 (Skull Mount Kits) which was the fourth full cycle of the sterilization validation runs had 26 of [redacted] packages of kits rejected due to seal burst during sterilization. The packaging sealer was revalidated but only empty packages were used for testing. No packages containing actual product were tested.

Two months later after the packaging process was revalidated, lot 0197 (Biopsy Kits) which were subjected to a 10 to 10½ hours ETO sterilization cycle had 51 of [redacted] kits rejected due to burst package seals after sterilization. The package sealer was again revalidated testing empty packages, not packages containing actual product.

The Computer Numeric Control (CNC) machines used to manufacture medical devices and their components have not been validated. For example, a [redacted] CNC machine is used to manufacture the aluminum T-nut (part 744A1367), a component of the Biopsy Kit. This machine has not received installation qualification and the process for machining the aluminum T-nuts has not been validated.

Failure to ensure that the disposition process for nonconforming products is adequately controlled.

The determination to use nonconforming components in production is not always based on scientific evidence. There were at least ten "Part Disposition Sheets" requesting acceptance of components which deviated from specification and there were no documented scientific justifications for the concessions.

Failure to establish and implement an adequate complaint handling program.

> Repairs to medical devices which are returned due to failure to meet specifications are not always viewed as complaints even when the problem is confirmed. For example, a repair (Control # 972184) to a Mayfield base unit, Lot 969R was returned due to the lever not holding or staying tight. The problem was confirmed and the device repaired but the repair was not considered as a complaint and no corrective action was considered and a "Compliant Report" form was not completed.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the FDA inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems you must promptly initiate permanent corrective actions.

In order to facilitate FDA in making the determination that such corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume marketing clearance, and export clearance for products manufactured at your facility, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that it has conducted an audit of your firm's manufacturing and quality assurance systems relative to the requirements of the device QSR regulation (21 CFR, Part 820). You should also submit a copy of the consultant's report, and certification by your firm's CEO (if other than yourself) that he or she has reviewed the consultant's report and that your firm has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant. The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates: November 1, 1998, November 1, 1999, and November 1, 2000.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the QSR deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by The Food and Drug Administration without further notice. Possible actions include, but are not limited to , seizure, injunction, and/or civil penalties.

The FDA inspection of your facility revealed that there were device-related complaints received by your firm that may be reportable to FDA pursuant to the Medical Device Reporting Regulations (MDR) for medical device manufacturers. The complaints involved the Mayfield Skull Clamps, Swivel Adapters, and skull pins. We have referred the complaint reports to FDA headquarters, Office of Compliance in the Center for Devices and Radiological Health (CDRH) for further review. At the close of the FDA inspection, management at your firm stated that you plan to report all of the complaints in question to FDA as MDR events by April 30, 1998.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

Your response to this Warning Letter should be sent to Evelyn D. Forney, Compliance Officer, Food and Drug Administration, 1141 Central Parkway, Cincinnati, Ohio 45202.

Sincerely,

Henry L. Fielden
Acting District Director
Cincinnati District